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Early diagnostics and Alzheimer's disease: Beyond 'cure' and 'care'

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ABSTRACT

Research on early diagnostics for Alzheimer's disease is supported by what has been labeled as aging-and-innovation discourse, in which innovation is assumed to (partially) resolve the societal problems related to aging. This discourse draws on a specific way of understanding Alzheimer's disease and ways to deal with this condition, namely a biomedical model of Alzheimer's disease, making the socio-cultural dimensions of Alzheimer's disease and aging less visible. In this paper we further scrutinize the various meanings of this innovation by analyzing how it is intertwined with different ways to define Alzheimer's disease and strategies to deal with it. We investigate interpretative packages in two distinctly different settings: a health technology assessment (closely related to the current research on early diagnostics) and Alzheimer's Cafés (where patients and their family meet). Eleven interpretative packages summarize the scope of ongoing deliberation in these two settings. By comparing and contrasting these interpretative packages we are able to better characterize how new health technologies are accompanied with definitions of the problem and forecasts of the future. We conclude that these interpretative packages about early diagnostics are less monolithic and host a variety of different, sometimes conflicting definitions of early diagnostics, the problem of Alzheimer's disease and its multiple futures.

1. Introduction: 'cure' or 'care'

A central assumption in policy circles and research funding is that scientific research and technological innovations provide answers to societal challenges of aging. This is also the case with innovation in the field of Alzheimer's disease. The argument is that due to an aging population the number of persons with Alzheimer's disease will increase drastically in the coming years and that this will lead to huge problems in the health care system and the economy. This crisis account of aging [1,2], is then turned into a major societal 'challenge' to be addressed by innovation. This way of reasoning has been found in general in relation to issues of aging and has been typified as the 'aging-and-innovation discourse' [3]. Early molecular diagnostics is one of the key innovations positioned as a step towards the (partial) solution, for example in the Dutch 'Deltaplan dementia' [4], the EU 'Joint Planning Neurodegenerative Disease Research Strategy' [5] and the US 'Alzheimer's Disease Neuroimaging Initiative' [6].

Early diagnostics here refers to both the possibility of an earlier diagnosis and the specific technologies to achieve this. The possibility of an earlier diagnosis can refer to different situations: an early diagnosis of dementia (as a cluster of symptoms and signs), a diagnosis of the pathology of Alzheimer's disease in a pre-dementia stage, as well as the diagnosis of Alzheimer's disease before any signs are present at all (called the asymptomatic stage) [7]. The specific technologies of early diagnosis are MRI scans, PET scans, and biomarker analysis.

The discourse and the underlying biomedical model have been criticized by many scholars in the past decades. According to the biomedical model, Alzheimer's disease is a condition of a person, caused by deterioration of the brain. Consequently, the way to deal with dementia is by medical

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control; although there is currently no cure, dementia should be diagnosed, managed and treated by medical authorities. The biomedical model has been critiqued for neglecting the social components, thereby affecting choices in policy and research, and having negative effects on the experience of living with dementia. Claudia Chaufan [8], for instance, showed how Alzheimer's disease as we currently know it has actively been constructed as a medicalized condition with a biomedical model of dealing with it. This "excludes alternative problem definitions" and has led to a "triumph of cure over care" in policy domains. In the same vein, Ingunn Moser [9] studied how Alzheimer's disease has been made to matter in different locations, among which parliamentary politics. She argued that "pharmaceutical and biomedical versions of the disease [are made] present, visible, strong and dominant", and alternatives are "made absent, invisible and less real" (pg 107). Care is not positioned as an alternative way of dealing with the matter, rather it is turned into 'doing nothing', an (expensive) option of last resort [9]. The prevalence of a biomedical model of Alzheimer's disease does not only affect policy, politics and division of resources, but is also critiqued for having negative consequences on the experience of living with dementia and on dementia care [10]. In reaction to the biomedical 'cure model', 'care models' emerged from the 1990s onward, with a main interest in the experience of persons with dementia, social settings and relationships. Thomas Kitwood is, for example, one of the pioneers of alternative models with his approach of person centered care [11–13]. He developed a broader framework for the understanding of dementia, not only including neuropathology but also social psychology, with the aim to provide good care and a better life for persons with dementia.

So, 'cure' and 'care' have appeared as two strategies to deal with Alzheimer's disease, with different overarching discourses and logics. In these critiques cure is defined as (aiming for) medical treatment, and care as 'alternative strategies', including provision of physical, practical, emotional and spiritual support. 'Cure' is often positioned as an 'oppositional construct' to argue the benefit of alternative approaches", [14] in [15] p.3. This positioning of cure versus care suggests that a choice needs to be made between a cure or a care approach: should one try to banish Alzheimer's disease from existence by investing in research to understand the causes of dementia and find a medical treatment, or should one search for the best ways to live *with* Alzheimer's disease and find ways to support patients and informal caregivers? In the cure versus care opposition, the prospect of early diagnostics becomes problematic. And when the underlying logics of cure and care are presented as opposites, a stalemate looms.

In this paper we investigate the various meanings of early diagnostics in society, and analyze how this is intertwined with different ways to define Alzheimer's disease and strategies to deal with it. The ongoing discourse on early diagnostics for Alzheimer's disease evolves and changes over time, and provides diverging meanings and interpretations for relevant events. A researcher may encounter all kinds of devices, like metaphors, images, arguments, and moral appeals. These different elements are not encountered as individual items, but they come in clusters, and are organized around a central organizing idea, and thus provide different, what Gamson and Modigliani refer to as, 'interpretative packages' [17]. We conceive discourse on early diagnostics for Alzheimer's disease as a set of interpretative packages, which make sense of early diagnostics. Distinguishing a set of interpretative packages creates room for a range of positions, rather than one overarching discourse, or two competing discourses. We scrutinize the meanings and assumptions by investigating interpretative packages related to early diagnostics and Alzheimer's disease. We define interpretive packages as clusters of topics, arguments, and concerns that are articulated recurrently in relation to the innovation and thus create a web of understanding, through which is made sense of this innovation.

We analyze these interpretative packages in two distinctly different settings where problems, solutions and futures are defined. The first setting, a health technology assessment project, is closely related to the research on early diagnostics, which can be typified as mainly a 'cure' context. The second setting, Alzheimer's Cafés, where patients and their family meet, provides contrasting 'care' perspectives and assessments of the disease and the ways to cope with it. We draw on literature from STS as well as from dementia care to unravel the different ways to deal with Alzheimer's disease and aging.

2. Theory: Alzheimer's and storytelling

The concepts 'dementia' and 'Alzheimer's disease' have a turbulent history of contestation. During the last century, the concepts have been the "*product of complex negotiation between a wide number of interested parties – including patients, caregivers, physicians, researcher, corporations, and policy makers – who all have a stake in how we perceive, name, and respond to illness*." p. 1 [16]. Contestations continue about how to define Alzheimer's disease and how to deal with it (see e.g. [10,11,18]). Is Alzheimer's disease a disease, or part of normal aging (e.g.[18,19])? What are the causes of the symptoms of Alzheimer's disease? It appears that persons with severe brain damage can experience little symptoms and the other way around. How can this be explained? And can changed behavior be considered to be the result of neurological deterioration, or to be the interplay between neurological impairment, physical health, and psychological and social factors [11]?

There are different ways to distinguish conceptualizations of dementia and ways to deal with it. The main theoretical models that are currently distinguished are a biomedical model, a psychosocial model, a disability model and a social gerontological model [15,20,21]. The biomedical model perceives dementia as a pathological condition that should be diagnosed and treated. It is characterized as an illness with progressive decline, of which you should recognize the symptoms and gain insight into the underlying causes. Since effective treatment is not available yet, it is of utmost importance to develop effective disease modifying treatment or preventative measures. A psychosocial model and a disability model put the person central and aim to increase the well-being of patients. The psychosocial model focuses on the consequences of dementia for individual persons with dementia and their caregivers. This leads to attention to the experience of the person with dementia and the strategy to adjust care and support, to better cope with this condition [15,22]. The disability model of dementia focuses on the irreversible limitations to the functioning of a person. These limitations or disabilities in daily functioning, ask for structural adjustments to rehabilitate and stimulate the person and for aids to keep persons functioning independently at a

certain level for as long as possible [21]. The social gerontological approach critiques the notion that elderly are a burden to society and deplores their social exclusion. It pushes the idea that life with dementia can remain fulfilling and points to the wider social and structural factors that shape the experience of dementia [15].

In current practices these different models do not exclude each other; they co-exist and relate to each other. Downs [20] speaks about an eclectic use of different models. As we recalled above, Moser stresses the politics at work in: how in certain contexts some modes-of-ordering are made visible, more real, and others are neglected, made invisible. And in her book *The Body Multiple* Annemarie Mol [23] describes how in different practices, illnesses are 'done' differently, or, in her terms, 'enacted'. For example, arteriosclerosis in the consulting room with a patient is something else than the entity derived from X-ray pictures of a radiologist. Also Innes and Manthorpe stress that "*How we approach dementia (…) will impact on how we 'see' the problem; how we might try to approach it; and how we might try and respond to or look for a solution.*" p. 8 8 [15]. It influences how not only professionals in health care, but also policy makers, persons with dementia, their caregivers and others respond to the challenges dementia poses on them. Innes and Manthorpe also note, however, that underlying assumptions and motivations are often implicit, blurred and multiple. The intricate relationship between the different versions and representations of Alzheimer's disease and the way to deal with it, is a central lesson of studies of medical practices in science and technology studies (STS).

Practices of dealing with a condition such as Alzheimer's disease are thus somehow structured. Annemarie Mol, for example, argues that medical practices are structured through ideals, such as the ideal of patient autonomy (the 'logic of choice') or through ideals of 'good care' (the 'logic of care'). These different ideals bring along "*a specific mode of organizing action and interaction, of understanding bodies, people and daily lives, of dealing with knowledge and technologies, of distinguishing between good and bad, and so on.*" p. 8 [24]. In her study of nursing homes, Moser emphasizes the performativity of 'modes-of-ordering': they make some responses or actions in a specific situation more appropriate, more logical, than others [25]. Different modes-of-ordering (she distinguishes a somaticing and a relational mode-of-ordering) shape how dementia is enacted upon, and along with this, shape the care for dementia, and the way of living and dying with dementia. Hence, there are more 'worlds-in-progress', while in different locations some might prevail different modes-of-ordering co-exist.

The meaning of early diagnostics for Alzheimer's disease as a way to deal with Alzheimer's disease in aging societies, is interwoven with the different understandings of Alzheimer's disease and ways to deal with this condition.

As an entrance to study the meaning of early diagnostics, and the connections being made between early diagnostics and ways of approaching and dealing with Alzheimer's disease we investigate the arguments, anecdotes and other stories that are shared and circulate in settings where Alzheimer's disease and early diagnostics are a topic of conversation. Storytelling is the way in which humans construct and make sense of the world around them and their own action [26–28]. Through stories meaning is created and shared. Stories create ordering by connecting different elements to a central purpose.

3. Methods

The central question of this paper is how the development of early diagnostics for Alzheimer's disease is entangled with specific definitions of Alzheimer's disease and articulations of problems and solutions in dealing with Alzheimer's disease in the (near) future. We do this by analyzing the various meanings of early diagnostics in two very different settings.

We investigate the meanings by distinguishing the 'interpretative packages' in the stories that are being told in different settings. We define interpretative package as a cluster of recurring topics, arguments, and concerns (thus different elements). These interpretative packages capture some aspects of early diagnostics in an ordered mode of understanding. They provide "webs of understanding" [29] to make sense of early diagnostics in a setting. Depending on the stakeholder, the topic and the kind of conversation, different interpretative packages can come up. These interpretative packages are constitutive for stories as they form a repertoire, which is available about early diagnostics. In different settings the repertoires may differ and some interpretative packages are more exotic to one setting than to the other. So interpretative packages are recognizable and recurring patterns of themes and elements that expose a web of understanding behind the development of early diagnostics.

We have selected two settings for this analysis, where sense is being made of early diagnostics and Alzheimer's disease through a vivid exchange of stories between different stakeholders. One setting can be considered to be more cure-oriented (a health technology assessment (HTA) working group within a biomedical research program); the other as more care-oriented (a series of Alzheimer Cafés in a Dutch city).

The HTA setting is part of research on early molecular diagnostics of Alzheimer's disease in the Netherlands that is taking place within the LeARN program (Leiden Alzheimer Research Nederland), and is partially financed by the ministry of Public Health. One of the conditions for this funding was clinical and societal relevance of the research. Therefore, the consortium devoted one work package to a health technology assessment (HTA) to evaluate the clinical and economic value of early molecular diagnostics. It inquires how different instruments perform, how much it costs and how the quality of life and health care costs change through the introduction of early diagnostic tests. This assessment includes monitoring a cohort of patients to measure the accuracy of different diagnostic instruments and the quality of life, a panel to determine the added value of these instruments in clinical decision making and a model to assess the costs of health care consumed by patients and their informal caregivers (with and without these novel instruments). Medical professionals (neurologists, psychiatrists, geriatrics, radiologists), chemical analysts, and health economists work together and exchange knowledge and ideas. Here we expected to find cure-related accounts with a medical, or evidence based approach to dementia.

The second setting is the Alzheimer Café. Alzheimer Cafés are monthly informal events for persons with dementia, their partners, family members, caregivers and other interested persons. They provide a space and time for the visitors to informally exchange ideas, information and experiences, and to provide support to individual persons with dementia or their relatives to help them deal with the situation. The Alzheimer Café was initiated in The Netherlands to tackle the

Table 1
Data sources for HTA.

Interview with Work Package leaders (1, 2, 3, 4)*
PhD students working on the HTA (5,6,7)*
Discussion meetings (8,9)*
(Draft) articles (10, 11)
Extended Work Package description (12)

*In collaboration with Anna Laura van der Laan.

taboo on dementia within society, between partners, and within families [30]. The concept of the Alzheimer Café quickly diffused across the Netherlands. Currently there are over 180 Alzheimer Cafés and their number is still growing. Also in other countries, such as the UK, the Alzheimer Café example is being followed [31]. The formal goals of Alzheimer Cafés are to educate, to speak openly about the problem, and to recognize and emancipate patients and family members. Every meeting lasts about 2 h and is organized around a theme (such as causes of dementia, dealing with dementia, communication) and led by a moderator [32]. Attendants of Alzheimer cafés consist of patients, their husbands, wives, friends, relatives, informal caregivers, volunteers, persons who are worried that they or somebody close to them is developing dementia, nurses, pastors, caretakers, municipality officials, general practitioners, and other local professionals. Everybody brings along their own experience, questions and knowledge on dementia and the way to deal with this condition. In this setting we expected to find care-related, person-centered and experience based accounts of Alzheimer's disease.

In both settings we collected different types of documents: reports, interview transcripts, articles, books, educational material, and notes and transcripts gathered through participant observation (See Tables 1 and 2). This diversity of data sources provides a rich pool of arguments, anecdotes and stories. We analyzed our documents with the following research steps. We first separated phrases (text blocks) that express (a) the role of early diagnostics (b) what Alzheimer's disease is and (c) what the future will bring and how to address it. Within this collection of phrases we labeled themes, such as 'stigma' or 'plaques in brains' or 'demographic trend'. We investigated how these themes are connected in the documents. In this way, we could identify clusters of connections, which we analyzed as different 'interpretative packages'. Next we summarized these different interpretative packages. The last step was to check whether all themes and connections were captured by the set of interpretative packages. For this process of labeling we used ATLAS.ti software.

Table 2
Overview of studied Alzheimer's Cafés.

Date	Theme of Café
April 2010	Dementia in different phases (13)
May 2010	Forgetfulness or dementia? (14)
June 2010	Early diagnosis (15)
November 2010	Film screening (16)
January 2011	Dementia and existential questions (17)
February 2011	Behavioral problems and dementia (18)
March 2011	The role of the general practitioner (19)
April 2011	Daycare and daytime activities (20)
June 2011	Case management for dementia (21)
October 2011	Applying for care and help (22)
November 2011	Auxiliary service (23)
February 2012	Occupational therapy (24)
May 2012	Behavioral symptoms of dementia (25)
June 2012	Healthy living (26)
November 2012	Dementia for the immediate environment (27)

The analysis of the Alzheimer Cafés is based on observations during Alzheimer Cafés in one region in the Netherlands from April 2010 until November 2012. During these cafés, the first author was allowed to make notes. Next to observing she also engaged in conversations with the visitors, and took on a similar role as volunteers of the Alzheimer Café. For background information about the philosophy, and organization of the Alzheimer Café she interviewed the organizers and participated in a course for volunteers of the Alzheimer Cafés. During all these occasions she made notes and transcripts.

While the analytical concern and the methodological steps in both settings are similar, the emphasis differs due to the nature of the settings. In the HTA setting early diagnostics and the solutions it could provide are more central, while in the Alzheimer Café setting, the emphasis is on dementia and how to deal with it.

4. Results

4.1. Setting one: health technology assessment

Health technology assessment is a standardized practice in health care to examine clinical, economic, societal and ethical implications of technologies in health care. It is intended as a bridge between medical research and policy making. While others have analyzed and criticized the limitations of the HTA approach (e.g. [32,33]), we consider this setting as an excellent entrance to gain understanding about what kind of solution early diagnostics provides, and how it is shaping and being shaped by enactments of disease and the way to deal with it. We could identify six interpretative packages of how early diagnostics is entangled with representations of Alzheimer's disease and how to deal with it. Our findings are summarized in Table 3.

4.1.1. Early diagnostics as value for money

The first interpretative package in the HTA practice views early diagnostics of Alzheimer's disease as a proposition about costs and benefits. This interpretative package concerns the efficient allocation of scarce resources in health care and is embedded in health economics. It can be summarized as follows.

"Health care is expensive and is getting more costly. New technologies could potentially improve health care and increase the quality of life for patients and informal caregivers, but may also lead to an increase in costs. Therefore, it has to be examined whether they are value for money. For early molecular diagnostics it is not clear yet."

This interpretative package centers on the advances made in imaging techniques and the analysis of cerebrospinal fluid in the past decade, leading to new and emerging diagnostic tests based on biomarkers, which could improve the diagnosis of Alzheimer's disease.

Table 3
Summary of interpretative packages in the HTA.

Setting 1: Health technology assessment				
Meaning of early diagnostics	Understanding of Alzheimer's disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
Value for money	Biomedical condition Highly affecting well-being of patient and informal caregivers. Societal burden	Increasing number of persons with dementia. Advances in imaging techniques and biomarker analysis.	More expensive health care. Decreased quality of life of patients and informal caregivers.	New cost-effective medical technologies. Decreasing societal costs. Increasing quality of life.
Changing health care	Biomedical condition Measurable or visualizable pathological changes in the brain highly affecting quality of life of patients and informal caregivers. Societal burden of increasing health care costs.	Increasing number of persons with dementia. Advances in imaging techniques and biomarker analysis. Maybe disease modifying treatment.	Increasing health care costs. Decreased quality of life of patients and informal caregivers. Uncertain consequences of early diagnostics in clinical practice.	Improve diagnostic accuracy. Increase health and well-being of patients and informal caregivers. Decrease societal costs. Assessments of consequences of early diagnostics in clinical practice.
Innovation trajectory	Biomedical Pathological changes in the brain that can be measured or visualized. Application area for imaging techniques and biomarker tests.	Progress through innovation.		Instruments to measure or visualize changes in the brain that signify Alzheimer's disease. Implementation of best technologies in clinical practice.
Changing definition of Alzheimer's disease	Biomedical condition Measurable or visualizable pathological condition in the brain. Dementia syndrome recognized by expression of a cluster of symptoms.	Ongoing development of imaging technologies and biomarker tests. Increased knowledge on pathological processes in the brain. Updated diagnostic guidelines.	Diagnosis based on symptoms.	Better predict disease progression. Provide diagnosis at an early stage, or predict disease, based on neuropathology rather than symptoms. Change diagnostic guidelines.
Step on the road to medication	Biomedical A presently irreversible, untreatable medical condition.	Development of disease modifying treatment.	Lack of disease modifying treatment. A distressing disease course. Far reaching consequences for the quality of life of patient and caregiver.	Progress in health care. Speed up development of disease modifying treatment. Diagnose the disease in early phase when medication is expected to be most effective.
Early management	Psychosocial Untreatable condition. Worry for persons with memory complaints.	More and more technological diagnosis.	Conducting a diagnosis as a goal in itself.	Diagnosis (better information) at a pre-dementia stage. Provide certainty to worried patients. Better management of the condition and patient in early stages.

While novel medical technologies could potentially provide benefit to patients and informal caregivers, they also contribute to the rising costs of health care. The task, thus, is to consider whether molecular diagnostic instruments have substantial added value for the patient and their caregivers, and whether they are cost-effective.

> "*Look, the whole reason why we are doing this research is because it is not clear if you should use these markers in the standard diagnostic procedure in the clinic or not." (5) "The HTA is about how much money you can put in to get how much quality back. And about how much money you can save by making an early diagnosis.*" (1)

In this interpretative package, Alzheimer's disease is considered as a disease that highly affects the well-being of patients and informal caregivers, and places a substantial burden on communities, given the rising number of persons with Alzheimer's disease in the near future, and the related rising pressure on health care resources. According to this interpretative package, it is of utmost importance to validate these new tests, in terms of patient well-being, costs, and on their additional value to current clinical practice.

(Sources: 1, 2, 5, 10, 11, 12.)

4.1.2. Early diagnostics as having uncertain consequences for (future) health care practices

A second interpretative package highlights the struggle with the uncertainties of the (future) consequences for health care practices, when newly developed early diagnostic instruments are adopted: How would these tests improve the accuracy of a diagnosis? What consequences does this have on the quality of life of a patient and the informal caregiver? What would be the consequences for health care costs?

It can be summarized as: "Consequences of new health technologies are complex to assess. You first need to know how they will change the possibilities for diagnostic and clinical practice, and what it means for patients, informal caregivers and the total costs of health care. It is a tremendous task, but we need to do it."

In this interpretative package the focus is on the chain of consequences to be measured and modeled in order to determine the influence a test will have on health, well-being and societal costs. This is a complex task involving many uncertainties. "*This is what we are after: what is happening exactly? What is being done with information from these tests? What does the whole process look like from adding a new test to, ultimately, the health effects*?" (8) To bridge the gap between research and clinical practice a lot of information and assumptions are needed: the technical quality of the tests, the performance in terms of sensitivity and specificity and predictive value, the value of a test if added to other tests, how this will change diagnostic decision making, how this effects treatment and patient management, and how this will affect health and well-being of patients and informal caregivers, and eventually what the consequences are for societal costs. With every step in this model uncertainties grow and need to be dealt with. "*When you add a different test, or change the combination or sequence of tests, this will lead to a different accuracy. The added value in accuracy can lead to different decisions in care which will lead to a certain health effect and use of means in healthcare (for example a decision to do follow up tests)*." (8)

In this interpretative package different pressing questions are voiced. The central worry here is choices need to be made about what will be included and excluded in the model before it 'explodes of complexity', as a researcher phrased it. Furthermore, tests need to have consequences for patient management. Since currently there is no disease modifying treatment, or care program available yet for these patients, what will be the added value for patient management? "*What will be the consequences for treatment? Which clinical decisions are taken based on the scan results? You have to take into account the intervention options. A test by itself does nothing. The most important is having intervention options. And the cost-effectiveness depends on the possibilities you have for that.*" (9)

Another issue is that while these novel tests are being assessed it is not yet clear what the outcome of a test means. Whether these patients will really develop Alzheimer's disease, and within what period, is part of this research and is not known yet. "*A: You might think it is malign to have a positive scan result, but the question is what relevance this has. If you say to a person: I am afraid you will function less well in … the term becomes important. Is three years important? Is two years important? (…) B: What is a useful outcome of test? Everybody knows they will function less well in 20 years.*" (8)

What to do with patients on whom you already conduct these tests, and that have positive biomarker or imaging test results, but show no deviation on neuropsychological examination? Should you tell them the results of the specific tests, while it is not clear what these results mean? And what do you have to offer them, besides a follow-up appointment? "*A: How do you currently deal with subjective complaints? Persons who do not have… (…) B: Sometimes it is being said that (…) the scan suits their age. They are often elderly patients and they can have deviations in the (…) scan without cognitive complaints. So we communicate it like that. (…) A: (…) So whether it is positive or negative, it is 'suitable to the age'. So really it doesn't make a difference? B: No, but it is the correct answer at this moment in time. On which you could ask the question 'than you shouldn't apply for a scan'. And of course that is a little bit the field of tension we are in now. Especially with subjective complaints. This is not really a clinical… it is a research question.*" (…) B: "*So there has to be a clinical indication for a clinical scan. That does not mean that I think it is important for a patient to hear the full 100% information from a scan, but I do think (…) it has to have consequences, even if it is just to see a patient a bit earlier on follow-up, or not at all.*" (8)

In this interpretative package, the task of HTA is to assess the value of these novel tests in clinical practice, which comes with the challenges of dealing with many uncertainties that need to be faced.

(Sources: 5, 8, 9, 10.)

4.1.3. Early diagnostics as innovation trajectories

A third way to view the efforts to develop early diagnosis of Alzheimer's disease is to position them as different competing innovations. Summarized: "Progress in health care is possible with innovation. Early diagnostics is an umbrella term for various technological developments. They are rooted in different sets of expertise. So, technologies have their own trajectories and they compete."

'Early molecular diagnostics' is an umbrella term for different innovative techniques such as MRI and PET scans as well as the chemical analysis of cerebrospinal fluid (CSF analysis). For these techniques some tests are established and used in clinical practice and a lot of them are still being developed. And for all these techniques many different kinds of tests are developed, focusing on different mechanisms related to Alzheimer's disease, different biomarkers, different structural deviations in the brain, or different ligands and radioactive labels (PET).

Within this interpretative package it is emphasized that these specific tests are developed based on long-time experience and expertise in either PET, MRI or CSF analysis, of the different medical centers that are involved. Not only are they experienced in the application of existing tests, but also in developing new diagnostic tests for neurological conditions. Also past experience of industrial partners has informed the choice for pursuing research on some specific biomarkers. Past performance has been an important driver for the creation of a new research program on early diagnostics for Alzheimer's disease. These tests for Alzheimer's disease are part of build up expertise in specific areas, and thus embedded in innovation trajectories and research lines.

In this interpretative package, the development of early diagnostics is considered as research and innovation, and comes with many obstacles, drawbacks, unexpected results and problems during the development. For each test that is being developed there are long chains of steps that are needed to actually have a test ready that could be evaluated on its diagnostic value. Some tests turn out to be not good enough; each test has its own strong points and weak points.

A central argument in this interpretative package is that a successful test, or combination of tests, could change the diagnostic practice a lot. This could have far reaching consequences. CSF analysis for example is relatively cheap

and samples of liquor (cerebrospinal fluid) could be easily send to a laboratory to be analyzed, which means it can be easily implemented in current diagnostic practice. If PET turns out to be the best, implementation is more complex and expensive, since broad application would create the need for PET scans in more hospitals, as well as facilities that can produce the radioactive labels that are needed for the PET scans.

(Sources: 1, 2, 3, 8, 9.)

4.1.4. Early diagnostics as changing the definition of Alzheimer's disease

A next interpretative package centers around the way Alzheimer's disease is defined and diagnosed and how novel technologies will change this. "We are now capable of diagnosing Alzheimer dementia at an earlier stage, which changes the notion of what it means to be diagnosed with Alzheimer's disease. But also the basis on which a diagnosis is made is shifting. The diagnosis of Alzheimer's disease used to be on the basis of exclusion of other conditions. The importance of early diagnostics is that it can show actual traces of Alzheimer's disease in the brain. In this way, the whole notion of Alzheimer's disease changes from symptoms to pathology. With early diagnostics we can work on better definitions for research, drug development and monitoring of patients."

This interpretative package resonates with a long standing concern in research on Alzheimer's disease. Alzheimer's disease is the most common form of dementia. Currently a person is diagnosed with Alzheimer's disease when he or she expresses the symptoms of dementia of the Alzheimer's type. This is a so called 'syndrome diagnosis'. MRI scans were mainly meant to exclude other conditions. Within these criteria the definite diagnosis Alzheimer's disease based on pathology (based on depositions and accumulation of the proteins amyloid and tau in the brain) could only be made post mortem, based on biopsy and autopsy.

The emergence and ongoing development of brain imaging technologies however, made it possible to study the changes occurring in the brain due to Alzheimer's disease not only after death, but during life. Early diagnostic instruments aim to signal changes in the brain that can accurately predict if a person will develop the symptoms of Alzheimer's disease or not. This could shift the clinical diagnosis from a diagnosis based on symptoms, to a diagnosis based on pathology during life. "*We can follow these parameters over time in a person. This is revolutionary within the thinking about Alzheimer's!*" says one of the leading scientists (3). "*I think in the future the bulk of the diagnosis will be molecular diagnostics. Molecular imaging and CSF analysis will eventually be a better predictor of the disease than symptoms.*", says another leading scientist of the LeARN program (1).

A good diagnostic test will have to be sensitive and specific. However, most tests (also not the ones currently used) cannot provide 100% certainty. A problem that occurs is that there is no complete correlation between the development of specific neuropathology and symptoms of Alzheimer's disease. There are for example persons with cognitive complaints who do not have amyloid plaques in the brain, and persons without complaints who do. What should be decisive in a diagnosis in those cases: the symptoms or the pathology?

"*C: And the question is how you look at Alzheimer's disease. Do you call it Alzheimer's disease if somebody has clinical symptoms, or if someone has Alzheimer pathology? A: That is exactly the key question. (…) We cannot solve that now, you could discuss about this endlessly.*"(8)

"*I think the whole idea; the whole thinking of Alzheimer's disease will change. And the lay person should also realize this. That is what we are already doing at the memory clinics, we say to people: you have Alzheimer's disease. And then they expect that they will be in a nursing home with a diaper between their legs. And then we have to say: no, it will not go that fast. Because in the old days we diagnosed the condition in a much later stage. Nowadays we can do it much earlier, in a milder stage, and for that reason it is so important to support you so you can live a good life for another ten years. So what you have been through with your mother, exactly that we will try to… But of course it remains a nasty condition, so you cannot go around that. But the idea that there is nothing you can do is… Successful dementia for example, well, ten years ago, you should not have come with such an idea, and I think that now, it is well possible to handle this handicap in successful ways. (…) I think the general image of dementia, of Alzheimer, will have to be adjusted. Because you are earlier with the diagnosis. So it is not that when you hear the A-word, it means the end.*" (1)

(Sources: 1, 2, 3, 5, 11.)

4.1.5. Early diagnostics as a step on the road to medication

Another interpretative package brings together diseases, diagnosis and medication. "Early diagnostics should lead to better medication. Progress in health care is about finding better medication. When patients are diagnosed more accurately, the matching of patients and drugs is better. Furthermore, an early diagnosis enables treatment at an early stage when medication is expected to be most effective. Even when treatment is lacking currently, it is important to anticipate its future availability."

In this interpretative package it is stressed that Alzheimer's disease is an irreversible disease with a distressing disease course and far-reaching consequences on the lives of persons affected by it, and that there is currently nothing that can be done about it. Medically speaking, in the present and near future, receiving an early diagnosis is of no use for it does not lead to specific treatment options. The ambition, therefore, is to make sure persons have a better life and end of life, by developing disease modifying treatment. "*To optimize the benefits patients can gain from treatment, installment early during the course of the disease is desirable. However, AD is characterized by a long preclinical course (accumulation of the histological changes is estimated to precede clinical symptoms for as long as 15 years). Due to the lack of symptoms during the early phases of the disease, early treatment will depend completely on diagnostic tests that permit early diagnosis. Such tests are currently lacking.*" (12)

If there would be disease modifying treatment, this should be provided to patients as early in the disease process as possible, for instance in the stage of mild cognitive impairment (MCI), when they do have memory complaints, but not yet

dementia. It should be possible to predict who will develop dementia in 2, 3 or 10 years. So, prevention is even better than cure. You cannot be too early to keep people healthy. "*A: If you talk about asymptomatic Alzheimer's disease, that is the wrong way to go. You should not call that a disease. Maybe an Alzheimer profile… but there is no benefit in labeling that a disease. That is essential now. B: Yes because there is no treatment. But that could be very different when there is a treatment available.*" (8)

In this interpretative package, early diagnostics and the development of treatment go hand in hand. The question is at what time from now a medical intervention will be developed. "*As soon as there are biological interventions possible, pills for example, then things will change drastically. Everybody would like to have a scan; there will be a massive run on that. The question is at what time from now that will happen. We have to be realistic, because we have been saying that it will happen in 5 years for 25 years now.*" (1)

Moreover, one cannot develop a good therapy without a good diagnosis. "*If you treat a population of patients with anti-Alzheimer drugs, but 20% of these patients actually do not have Alzheimer's disease, you will never find a medication that can treat Alzheimer's disease*.", says one of the senior researchers (3). A good diagnosis is needed to test new medical treatments. And when a new treatment would become available, diagnosis is of utmost importance to provide it to the right patients.

So the importance of the development of early diagnostics is to speed up the development of treatment and to provide treatment to patients in an early stage. "*This is what justifies the whole research so far.*" (3)

(Sources: 1, 2, 3, 12.)

4.1.6. Early diagnostics as part of early management

This interpretative package addresses how early molecular diagnostics can benefit patients in the present, with no disease modifying treatment available. "The quality of new technologies for health care is determined by its benefit for patients. Since there is no medication for Alzheimer's disease, early diagnostic technologies have nothing to offer in terms of cure. Instead, early diagnostics should be part of management of the disease in early phases."

This interpretative package contains the criticism that the diagnosis seems to be becoming a goal in itself and does not answer the question what is the use of it for a patient. Scientific research to make amyloid visible in a 7 Tesla MRI scan for example, can be meaningful in itself. "*But if you translate this to the interest of the patient, you have to be honest. Scientific insights can be of interest for the patients, eventually. That is, for the patient 'in general', not for the individual patient in the present.*" "*You should not sell science as good patient care.*" (1) For the present patients, "*It is not about the diagnosis, it is about what you do with it. Early management, not early diagnosis. I think there is too much focus on diagnostics as a goal in itself, which is typical.*" (1)

Currently a lot of tests are conducted to support a diagnosis. These tests are synthesized by a physician who will diagnose the patient, that is, when somebody already has symptoms of dementia. But with early diagnostics, when the symptoms are still subjective, persons are most worried, about whether this is just a temporary problem, or that it will develop into a dementia.

In this interpretative package, the aim of early molecular diagnostics is to provide better information at an earlier stage of the condition, when patients can still understand and comprehend the diagnosis and what it entails. It provides possibilities for patients, informal caregivers, and professional caregivers to better manage the condition: to timely make plans, and arrange care and support. "*There is a danger that the care will be backgrounded. That a diagnosis becomes a goal in itself, and that persons will not be supported enough afterwards. So our plea is that a diagnosis should always be coupled to care. You cannot put somebody in a scanner (…) and then say — yes we found it. It has to have consequences. You can already see this happening as well. It will become more technological, but there is also much more care available than 10 years ago: memory training, education, informal caregiver support, Alzheimer cafés. So these developments go hand in hand. This research program is about the technical side.*" (1)

(Sources: 1, 2, 3, 8, 9.)

4.2. Setting two: Alzheimer Café

The second setting we used is the Alzheimer Café. Alzheimer Cafés are installed to help persons who are faced with dementia to better cope with this condition. Many local professionals attend these meetings, as well as patients, their caregivers, family and friends, and persons who are worried about dementia themselves, or that a loved one might be developing dementia. This setting might not be the most obvious place to learn about early molecular diagnostics. It is a non-medical setting, and seems distant from technological developments. Yet, here new technologies are on the horizon as well, so it is an interesting setting to study to understand how the development of early diagnostics is interwoven with specific definitions of Alzheimer's disease and articulations of ways to deal with Alzheimer's disease. In the discussions, lectures and conversations in the Alzheimer Cafés we could identify five recurring patterns of which we constructed the following interpretative packages. Our findings are summarized in Table 4.

4.2.1. Early diagnostics as identifying a biomedical condition

The first interpretative package relates to the understanding of memory complaints as a foretoken of Alzheimer's disease, which should be diagnosed by a doctor. "In case of worries about forgetfulness, go and see your doctor. With new diagnostic test a diagnosis can be conducted in an increasingly early stage. Alzheimer's disease is a disease of which forgetfulness is an important symptom. However, it is not the only cause of forgetfulness, so it is important to find out what is going on."

In this interpretative package it is stressed that the most well-known first indicator of Alzheimer's disease is forgetfulness. Forgetfulness can have many underlying causes, like depression, stress, normal aging, and use of alcohol, but it could also be the first signs of dementia. The question is when forgetfulness is the first sign of Alzheimer's disease. To find out what the causes are of the complaints, a person can go to a doctor or a memory clinic. "*Alzheimer is a medical*

Table 4
Summary of interpretative packages in the Alzheimer Cafés.

Setting 2: Alzheimer Café				
Meaning of early diagnostics	Understanding of Alzheimer's disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
Identifying a biomedical condition	Biomedical Progressive disease of plaques and tangles in the brain, that leads to dementia. Of which forgetfulness is a foretoken.	Predict which patients with subjective complaints or mild cognitive impairment will (not) develop dementia.	Late diagnosis. Misunderstandings. Unnecessary worries.	Early signaling and diagnosis. Provide a prognosis, comfort, prevent misunderstandings, regulate risk factors, receive available treatment, organize care and support, plan life.
Part of good patient management	Psychosocial/disability A disease with many faces.	Providing care and support means searching and trying what suits these persons in this situation. There are hardly ever real solutions.	Exhaustion of informal caregivers. Crisis situations. Unnecessary suffering.	Timely provision of care and support that suits these persons in this situation. Adapt life to the new prospects. Improve coping with the condition. Improve daily life. Enable staying at home as long as possible.
Attributing a (socially significant) label to a person	Social gerontological A culturally laden label. A taboo.	Diagnosis at an increasingly early stage.	Mismatch between social perception and actual functioning of a person. Taboo. Stigma. Disqualification or social exclusion of persons with Alzheimer's disease.	A confirmation and reassurance. Foster understanding about dementia. Psycho-education. Reduction of taboo. Social inclusion.
A life event putting things in the 'Alzheimer perspective'	Psychosocial/Life event Certainty of a tragic fate. A means to reinterpret past events and to adjust life plans.	Changed prospects on life. A certain and continuous process of far reaching loss Increasing care responsibility for close relations.	A paternalistic notion of knowing what is good for a person.	A changed prospect on life. Respecting coping mechanisms of a person. Know what you are up against. Recognition.
Reducing the societal burden	Societal burden Burden on health care costs and health care system. Biomedical/psychosocial A need to provide timely care and support to patients and informal caregivers.	Increased number of patients with dementia. Increased health care costs. Budget cuts in health care. Worries about availability of care and support in the near future.	Misunderstandings. Crisis situations. Patients and informal caregivers falling between two stools. Gap between an early diagnosis and the access to professional care and support.	Timely signaling of signs of dementia. Timely organizing care and support. Availability of payable care and support. Delayed uptake in nursing home/stay at home longer. Increased use of social network of patients to provide care and support.

diagnosis. In the pre-stages of Alzheimer you cannot speak of dementia, but you can speak of mild memory problems, which in some cases will lead to dementia. It is difficult to interpret. Also other complaints can be a foretoken of dementia, such as changes in character or behavior. This depends on the type of dementia." (14)

In a memory clinic a set of tests will be conducted to distinguish if complaints of the patient or his/her relatives might be related to normal aging, mild cognitive impairment (a gray area of more complaints than can be related to aging, but less than dementia), or dementia. And what the underlying disease process is (Alzheimer's disease, vascular dementia, or something else). "*The more research with scans progresses, the better they can distinguish one dementia from another.*" (20) The patients receive a diagnosis: 'you are overly worried, you function very well', 'you have normal forgetfulness related to aging', 'we understand you are worried, it is not completely normal, but the complaints are not severe enough to speak about dementia' or 'you have dementia of a certain type'.

> "*Often persons visit the memory clinic who are needlessly worried. There is so much information about dementia, that this leads to fear (…). Forgetting something is normal when you age. Forgetting the name of your grandchild once is normal, as forgetting a card in a game of bridge once in a while.*" (19)

In this interpretative package the importance of an early diagnosis is to provide a prognosis, to comfort persons that are overly worried, to prevent misunderstandings, to regulate risk factors such as high blood pressure, and to provide treatment with the medication that is available. For good management of this condition, it is important that after a patient has received a diagnosis, (s)he moves into a care trajectory.

In this interpretative package it is stressed that there is still uncertainty and lack of knowledge concerning the causes and mechanisms involved in Alzheimer's disease. Researchers all over the world are working hard to better understand this condition and to find ways to stop or slow down the progression. Current research is aimed at early diagnosis: predicting which persons with subjective complaints or with mild cognitive impairment will develop dementia, and which won't. Scientific research now conducted aims to improve these predictions. Next to this a lot of research is directed at the development of drugs to stop or slow down disease progression, but so far nothing really works.

(Sources: 13, 14, 15, 19, 22, 23, 24, 25, 26.)

4.2.2. Early diagnostics as early patient management

This interpretative package is about how patients and informal caregivers can best cope with the changing situation which comes with the gradual changes related to Alzheimer's disease. "It is key that patients and informal caregivers make sense of early signals of dementia and can adapt their life to this new situation and related prospects. An official diagnosis should support their understanding and provide entrance to health care arrangements. The core issue of Alzheimer's disease is how patients and caregivers can cope with it."

> "*A lot has changed in the past decennia in the attitude towards dementia. In the past people pretended as long as possible that there was nothing to worry about. Dementia was seen as a verdict, where there is nothing to be done about. Now we want to know what is going on as early as possible, to try to slow down symptoms and prepare for what is ahead: disease wise, but also for the person and the family, and make a support plan around that person and family.*" (19)

> "*Guest: What if mom does not want to see a general practitioner? Speaker: That is a matter of collaborating. You could for example try to go to a general practitioner with other complaints and slip it in. You can also visit the general practitioner yourself. A plan needs to be made. The worst thing you can do is pretend that there is nothing going on.*" (19)

There are different organizations that offer their help to find out what is going on and to make a plan of what is needed to keep on functioning in your daily life and live independently (e.g. the elderly welfare organization, or a case manager). The argument is that a lot of support, care and help are possible when faced with the prospect of dementia. However, when coping with dementia and problems related to dementia, there are hardly ever real solutions. Providing good care involves searching and trying what suits the persons involved and their situation.

Yet, there are so many rules, laws and administrative procedures, that obtaining help is quite complex. For reimbursement and access to the professional care and support available, often a diagnosis dementia is needed. This means that there is a need for a timely diagnosis — not too late and not too early. A timely diagnosis means entrance to a care trajectory, precepts and guidelines and avoids that the informal caregiver becomes exhausted.

> "*I talk to a couple before the café starts. The woman tells me that she received a diagnosis Alzheimer two months ago. She already knew she had Alzheimer's and had been to the general practitioner, who would not refer her to a memory clinic. Even her bridge partners knew it. She was not able to play bridge anymore. She forgot all the cards. (…) Eventually she went to another general practitioner who send her to the memory clinic. There, the scan showed that it really was Alzheimer's. The doctor (…) had fully understood her. He had asked if she wanted to hear the diagnosis, and she had said yes. It will make you calmer, the doctor had said, and that was exactly the case. Now she has the confirmation that she is not crazy, and that she really has Alzheimer, which she had expected all the time. Now, she says she gets Exelon plasters and goes to a daycare four times a weak. She looks optimistic and relieved. Her husband looked like he was not as relieved as his wife. I asked him if the diagnosis had also made him calmer. No, not really, he said. I asked if things changed for him afterwards. Also not, he replied. It is very difficult at home. She is so aggressive. It is very heavy.*" (20)

In this interpretative package Alzheimer's disease is portrayed as a disease with many faces. The disease progresses differently in individuals. The specific symptoms and the speed in which the disease progresses differ from person to person. And different persons cope in different ways with this condition. Some individuals may panic, some accept it easily, and others are calm and even happy. To organize good support and care for everybody involved, timely signaling of problems and receiving a diagnosis is deemed very important.

(Sources: 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27.)

4.2.3. Early diagnostics as labeling persons

In this interpretative package, the diagnosis Alzheimer's disease is not as much seen within the medical or health care domain, but in the social domain. "Now that Alzheimer's disease is diagnosed at an increasingly earlier stage, the mismatch between the public perceptions related to the label dementia and the actual functioning of a person will increase. A diagnosis Alzheimer's disease attaches a label to a person. When this happens, it has various profound social consequences."

A diagnosis means that a person is labeled with a certain condition. Alzheimer's disease is an attribute of a person which not only identifies the disease a person has, but also labels the whole person with this condition.

In the cafés it was articulated that this label can result in different responses. Depending on the persons involved, a diagnosis may come as a confirmation and reassurance and reduces uncertainty and bring understanding. On the other hand, a diagnosis can function as a stigmatizing label, disqualifying a person, by for example when relatives start talking in their place, or taking tasks of their hands. A woman came to the café to share the positive experience she has with the day care facilities for her mother, although "*her mother prefers not to speak about the dementia. She wants to function*

within normal life and she does not want to draw too much attention to the symptoms of dementia." (20) In a café about early diagnostics, I ask the question whether the visitors would like to have a diagnosis at an early stage. A response is that you should consider what this is like for the patients. "*I am afraid to be set aside with a 'label'*", says one of the visitors of the café. (15) The facilitator responds that this is often the case, but that this label can bring peace as well. "*Without it irritation may occur: "She forgot it again".*" (15) Symptoms of dementia can be interpreted as slackness, inattentiveness or unwillingness. To avoid the negative effects of a label in the home situation, psycho-education is very important for the patient and their close relations. They have to find the right path together.

This interpretative package emphasizes that "*because there is a lot of attention for dementia and because of new technological possibilities, people visit a doctor earlier and a diagnosis Alzheimer's disease can be given at an increasingly earlier stage of the disease progression. Because of that persons who are diagnosed with dementia now are still capable of much more than in the past.*" (15) This means that the public understanding of Alzheimer's disease might not coincide with the functioning of a person who is diagnosed with this condition. One of the aims of organizing Alzheimer Cafés is to reduce this taboo, to talk about dementia, and to foster understanding that persons with dementia are not crazy.

(Sources: 14, 15, 23, 25.)

4.2.4. Early diagnostics as a life event putting things in an 'Alzheimer perspective'

In the next interpretative package, the knowledge of having Alzheimer's disease that comes with a diagnosis, becomes an important element in the story of the life of persons with dementia and their close relations. "Being diagnosed as having Alzheimer's disease is a life changing event. It requires a deep existential response and changes a person's past and future. Do you really want to know this in an early stage?"

Expectations about life change drastically and certainly when diagnosed with Alzheimer's disease. Facing Alzheimer's disease signifies facing a certain and continuous process of far reaching loss for the patient and their close relations. Dementia is a terrible disease and a tragic fate.

> "*I enter the café, it is still early and I join a lady who sits alone at a table. She tells me her husband has been diagnosed with early stage dementia recently. How was it for you, to hear the diagnosis, I asked. Well that was a huge shock. (…) We now know what is going on, but it also gives other prospects. Not quite rosy. I just retired. I am 67. My husband is older. But still…*"(26)

In this interpretative package it is highlighted that persons who are faced with this condition need to reconsider the prospects on their lives, in the light of this dismal future they are facing. "*My husband has early stage dementia, which was diagnosed 1,5 year ago at the memory clinic. When we heard it, it felt like a verdict. And that is what it is. It feels like we are having Alzheimer together. My husband is very open about it; sometimes he says 'I happen to have Alzheimer'. He also told it to our children, his brothers, sisters and friends. It makes it easier to talk about and also to make jokes about it.*" (27)

Close relations, who are faced with the great responsibility to provide informal care to the person with dementia, are up against a huge and burdensome task, accompanied by grief, anger, sadness, and feelings of guilt of falling short. Not only the prospects on life are reconsidered, there is also a move to look back to reconstruct 'when it started', and to put past events in the light of this newly gained knowledge.

In this interpretative package, questions arise concerning the desirability of these prospects on life at an early stage. Would you like to know if you or your relatives are developing dementia? And when? Are the little things mum forgets and her restlessness when your father is not at home, a first symptom of dementia? When your father has had Alzheimer, will you also get Alzheimer?

For some patients the diagnosis comes as a recognition of what they expected (or dreaded) and a relief that at least now they know what they are up against. But there is also a tendency to avoid such knowledge: "*I would like to be ahead of problems, but on the other hand, I would not want to know either*". (14) Often persons deny changes and refuse to see a doctor. Should the family respect this, or should they seduce the person to see a doctor for his/her own good?

In our current health care system, the idea is that persons should know what is wrong with them and that a person should receive a diagnosis, honest and clear. This has not always been the case. "*Should everybody be told this 'truth'? Do we always have to tell? It is very understandable to deny as long as possible that something is wrong.*" says one of the care professionals in a café. (16) Is it always good to tell the truth, seen that reactions to a diagnosis differ greatly? Do you want to face this truth early on, or live in ignorance (or denial) as long as possible?

(Sources: 13, 14, 15, 16, 19, 20, 21, 22, 23, 25, 26.)

4.2.5. Early diagnostics as reducing health care costs

This final interpretative package relates to the reduction of health care costs, which is necessary with the prospect of the increasing number of persons with dementia and the subsequent pressure this puts on health care and the economic system. "A timely diagnosis can reduce health care costs by preparing care givers and thus allowing patients to stay home longer. In an aging society, patients with Alzheimer's disease are a burden. Demographic trends will run to financial and nursing limits."

This interpretative package starts in a similar way as the aging-and-innovation discourse: In the coming years the number of persons with dementia will increase, while the number of persons to be able to provide care will decrease. This is because persons get older on average, and the baby boomers are aging. A timely signaling of problems that may be first signals of dementia is important, because this can avoid misunderstandings and crisis situations, by timely organizing support and care. A lot of care and support is available at the moment. This enables persons to stay at home longer, and reduces the need of expensive nursing homes.

Some visitors of the cafés expressed the worry that they do not want to be a burden for their children or society. This is accompanied by worries about how long care and support will stay available and payable, given the budget cuts in support and care at home. "*You have told us all about these*

possible forms of support and care that can be provided, but will this stay available, and for how long? Financially? With the budget cuts? We read all about it in the newspapers. We cannot afford it ourselves." "*I am really worried about the future*." A care professional says "*We are all searching to find the best way within the budget cuts." "But despite this, it is very important that you keep asking for help when you need it. Do not let rumors about budget cuts, or a decline of a help question scare you off.*" (22)

(Sources: 15, 16, 18, 20, 21, 23, 26.)

The table below summarizes the different interpretative packages and how they are related to understandings of Alzheimer's disease, what the future will bring and how to address it. When in the understanding of Alzheimer's disease one of the models of dementia is prevalent this is added in the column on this topic. Next to these models (biomedical, psychosocial, disability, social gerontological) we also found the understanding of Alzheimer's disease as a societal burden, as an application area of new technologies and as a life event, which could not easily be related to the models that were described in the introduction. Probably this is because the original four models mainly evolved in relation to patients, where in this article the innovation is central, and thus other considerations come to play.

5. Discussion and conclusions

Research on early diagnostics of Alzheimer's disease does not only bring new findings and promising technologies, but also introduces and reinforces particular definitions of the problem and forecasts of the future. In this paper we studied the various meanings of early diagnostics, how they are related to understandings of Alzheimer's disease and to strategies to deal with Alzheimer's disease in the future. We did so by studying in two different settings: a health technology assessment group and a series of Alzheimer Cafés.

First of all we can conclude that a broad variety of articulations is present, in both settings. This finding is in line with the literature on medical practice, which has stressed the different ways in which diseases are represented, understood and enacted.

Secondly, we found that, notwithstanding this variety, the huge diversity of ideas appears to be clustered. We have captured these as generic interpretative packages, which provide webs of understanding of the meaning of early diagnostics, related to what Alzheimer's disease is, and how we may envision efforts to deal with it in the future. A particular understanding of the disease tends to be related to a particular approach to cope with the situation, and with a particular idea on what the contribution of early diagnosis could be. In total we have described eleven interpretative packages, six in the setting of HTA and five in the setting of Alzheimer's Cafés.

Thirdly, in the different stories (the research data) that this analysis is based on, we found that in one conversation, during one meeting, or in one interview, more interpretative packages come up. So each individual interview or meeting can be viewed as a string of interpretative packages that are articulated. People move between different interpretative packages. The interpretative packages can be considered the 'beads' and every story a unique necklace.

While this clustering in eleven interpretative packages is a huge reduction in itself, and they are simplified and purified to some extent, our findings differ from earlier accounts which stress two opposing views, or logics, of health care. The first is a view which portrays a disease and its problems as a biomedical puzzle, to be solved by medical interventions and further medical research. The other, opposing view, portrays a disease and its problems as a condition of a person, to be dealt with through careful attention to the personal situation of the patient and his or her family. The first pole has been labeled as stressing 'cure', the second as stressing 'care'. This bi-polar condition is unfortunate and distorts a rich and sensible reflection on how to deal with diseases such as Alzheimer's in an aging society.

Our findings, however, go beyond this dichotomy of 'cure' versus 'care'. We did not find two logics at work, but eleven. A division in 'cure' and 'care' and models of Alzheimer's disease such as the biomedical, psychosocial, disability or social gerontological model, are based on how to best support and help patients and informal caregivers. However, we also found interpretative packages about the competitiveness in technology development and about innovations looking for application areas in clinical practice, about shifting notions of what is considered as normal aging and what is considered pathological, an interpretative package about the aging populations and the increasing number of persons with dementia that put a stress on the current economic and health care system, as well as a interpretative package on expectations about life and existential questions arising with a diagnosis Alzheimer's disease. Within developments of early diagnostics more comes to play, besides supporting or helping patients and informal caregivers. Of course, when we would have chosen other settings we may have found less or more, or slightly different interpretative packages. The basic lesson, however, is that when stakeholders reflect on early diagnostics there will be more than just two sets of positions, concerns and understandings.

We found that the envisioned implications of early diagnostics are entangled with cure and care strategies in various ways. First of all, early diagnostics is said to contribute to both the cure and care strategy, and thus making a cure versus care discussion less relevant. The co-existence of both approaches has been elaborated on before e.g. as co-existing in memory clinics when dealing with early stages of dementia [35] and in nursing homes [25]. Secondly, with a focus on early diagnostics more comes to the fore than consequences for patients, such as the organization of the health care system, and medical research agendas. Furthermore people with a diagnosis Alzheimer's disease are not mere *patients*, but also *persons* with a life and a view on life. We claim that a cure/care dichotomy brings along a narrow focus on how to deal with dementia, which obscures other interests, such as leading a fulfilling life, keeping a viable health care system, scientific advancement, or innovative competitiveness. Such considerations are equally important and should not be backgrounded.

In terms of the aging-and-innovation discourse, our analysis of interpretative package confirms that early diagnostics for Alzheimer's disease is not a self-evident part of a solution to the increasing number of persons with Alzheimer's disease in aging societies, such as the Netherlands.

The aging and innovation discourse mobilizes interpretative packages on reducing the societal burden, it emphasizes the importance of early diagnostics as a step on the road to medication, of identification of a biomedical condition, of changing of health care and of early management, and of progress through innovation. It leaves out how exactly early diagnostics will become part of good patient management, uncertainties about the value for money, worries about budget cuts in care provision and reimbursement, the uncertainties about the value of early diagnostics while disease modifying is not yet available, the (social) effects of the label Alzheimer's disease for a person, the life event this signifies, and how this changes the definition of Alzheimer's disease.

The two settings we studied provide richer accounts than the aging and innovation discourse. Both settings stress the importance of an early diagnosis as the identification of the condition underlying symptoms such as forgetfulness, as well as the need to timely provide care and support. But the social gerontological approach and the life event that a diagnosis of Alzheimer's disease entails are absent from the health technology setting, just like the discussion about the performance of specific diagnostic instruments, and shifts in the definition of Alzheimer's disease towards a more neuropathological definition are absent in the Alzheimer Café. The two settings thus seem to be complementary — a finding with practical and optimistic consequences. Instead of a paralyzing stalemate between 'cure' and 'care', the understanding of the problems and the ways to address it will have various overlaps. The theoretical and practical task ahead, thus, is not to articulate the two positions of 'cure' and 'care' further, but to map the overlaps of interpretative packages and thus to reconcile concerns and strategies. Another, less optimistic, conclusion would be that some interpretative packages are less visible, appropriate, or maybe even silenced in the modes-of-ordering present in these settings.

The richness we encountered, however, does not imply that the tension between 'cure' and 'care' as two fundamentally different modes of representing health care has vanished completely. However we did not encounter 'cure' and 'care' as two sets of parties that confront each other, or two bodies of argumentation. The tension between care and cure does not appear as two poles, but as a theme that submerges in many different interpretative packages. The polarization only occurred occasionally, when the allocation of research budgets or the attraction of patients was discussed, the cure–care opposition was used to mold the discussion and to mobilize allies.

To conclude, we can expect that every narrative about early diagnostics will mobilize some of these interpretative packages in particular ways and will leave out others, as part of politics, agenda-setting or the acquisition of resources by stakeholders. Our study emphasizes that different ways of approaching Alzheimer's disease are closely connected to the way we 'see' the problem and respond to it, or look for a solution. The explication of eleven interpretative packages creates the possibility to identify which ones are mobilized and which ones stay outside of discussions, arguments and conversations, and thus can serve as a way to understand the politics at work and identify and detect overlooked issues that should be included.

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